

REMARKS

In order to expedite the prosecution of the present application, Claim 1 has been amended in order to more particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically speaking, Claim 1 now requires that the optically active polymer compound be insolubilized through exposure to 50-500 kGy of  $\gamma$ -ray radiation. Support for this amendment can be found on page 9, second full paragraph of the clean copy of the specification. No new matter has been added.

Claims 1, 3-5, 13 and 15 have been rejected under 35 USC 102(b) as anticipated by or, in the alternative, under 35 USC 103(a) as obvious over Francotte. Claims 1, 3-5, 13 and 15 also have been rejected under 35 USC 103(a) as being unpatentable over Francotte in view of Voute. Claim 15 has been rejected under 35 USC 103(a) as being unpatentable over either Francotte or Francotte in view of Voute and further in view of either Ohnishi or Japanese Patent No. 2001-296288 (JP '288). Claims 1, 3-5, 13 and 15 have been rejected under 35 USC 102(b) as being anticipated by or, in the alternative, under 35 USC 103(a) as being obvious over JP '288. Claim 3 has been rejected under 35 USC 103(a) as being unpatentable over JP '288 in view of Francotte. Claims 1, 3-5, 13 and 15 have been rejected under 35 USC 102(e) as being anticipated by or, in the alternative, under 35 USC 103(a) as being obvious over Ohnishi. Claim 3 has been rejected under 35 USC 103(a) as being unpatentable over Ohnishi in view of Francotte. Applicants respectfully traverse these grounds of rejection and urge reconsideration in light of the following comments.

The presently claimed invention is directed to a separating agent for enantiomeric isomer. The separating agent comprises an optically active polymer compound carried on a porous carrier. The optically active compound has been insolubilized through exposure to 50-500 kGy of  $\gamma$ -ray radiation.

The separating agent of the present invention is used in the separation of enantiomeric isomers and has a high optical resolution power and a high solvent resistance. Due to the exposure of the optically active polymer compound to 50-500 kGy of  $\gamma$ -ray radiation, a different crosslinked structure is produced from that produced through ultraviolet radiation. This results in the separating agent having an improved separation ability over conventional separating agents disclosed in the prior art.

The separating agent of the present invention is a chemically bonded type separating agent, i.e. a crosslinking type. The chemically bonding type separating agent has an improved resistance to a solvent since it contains a polysaccharide structure which has been influenced through the chemical bonding.

Another type of separating agent is known as the coating type which typically has superior separation power when compared to the chemically bonding type of separating agent. The separating agent of the present invention, although it is a chemically bonded-type separating agent having a high solvent resistance, also has an equivalent separation power with that of the coating type of separating agent. This is completely unexpected in the art of chemically-bonded type separating agents and patentably distinguishes the presently claimed invention over the prior art cited by the Examiner.

The Francotte et al. reference discloses photochemically cross-linked polysaccharide derivatives which are used as carriers for the chromatographic separation of enantiomers. This reference discloses the use of ultraviolet radiation to cure cross-linked polysaccharide derivatives. As will be shown below, the present invention, which utilizes gamma-ray radiation to accomplish the cross-linking of the polysaccharide derivative has unexpectedly improved separation abilities as compared with other chemically bonding-type separating agents outside of the scope of the present claims, such as the cross-linked separating agent of Francotte et al.

The Voute et al. references discloses small dense microporous solid support materials comprising dense microporous mineral oxides matrices in which a skin of polymers is rooted, and their use in downstream processing, especially for fluidized bed purification of bioparticles or high molecular weight macromolecules. This reference discloses the polymerization of organic products using either UV light, gamma irradiation or microwaves. This reference also discloses that temperature may also be used to induce cross-linking or copolymerization of the monomer solution. Therefore, this references discloses the equivalency of different type of cross-linking inducers in the manufacture of a solid support material which is not shown to have a utility for enantiomer isomers, as required by the present claims. As will be discussed below, in the present utility of separating enantiomeric isomers, the use of gamma ray radiation provides expectedly superior properties in the separating agent. Therefore, Voute et al. in combination with Francotte et al. does not negate the patentability of the present claimed invention.

JP '288 and the Ohnishi reference both disclose fillers for separating optical isomers in a liquid chromatography process. The fillers have a primary constituent of a polysaccharide derivative which can be bonded on a support by chemical bonding irradiation with gamma-rays, electromagnetic irradiation with microwaves or a radical reaction using a radical initiating agent. Neither of these references have a specific example which discloses the use of gamma-rays to immobilize a polysaccharide derivative on a support. These references add nothing to the previously discussed references and, as shown below, the presently claimed invention is patentably distinguishable over any combination of the references cited by the Examiner.

As discussed previously, even though the separating agent on the present invention is a chemically bonding-type separating agent, it is provided with an unexpectedly improved

separating power as compared to other chemically bonding type separating agents, such as the cross-linked polymeric separating agent of Francotte et al. It is well known in the art, that coating-type separating agents, although they have high separating properties, have no resistance to a solvent, which tends to dissolve the polysaccharide. Comparative Examples 2 and 4 of the present application show this. The treated agents lost their separation ability after the passing of the THF solvent. In contrast thereto, Examples 4 and 7 of the present application show that the inventive separating agent retained their separation abilities even after being washed with THF.

In the references cited by the Examiner, whenever gamma-ray radiation was mentioned, it was disclosed as being equivalent to other methods of accomplishing cross-linking. As shown in the table enclosed with the previous response, Examples 17 and 18 in the table correspond to the Francotte et al. reference where the cross-linking was performed by ultraviolet radiation. A comparison of Examples 17 and 18 with the examples of the present invention clearly show inferior separating properties. On the other hand, when the separating agents of Comparative Examples 2 and 4 were not cross-linked and washed with THF, it did not show any separating properties. Therefore, through the cross-linking of the chemically bonding-type separating agents of the present invention using gamma-rays, Applicants are able to provide the unexpectedly high separation ability associated with the coating-type separating agent and yet possess the resistance to a solvent shown by the chemically bonding-type separating agent. This is clearly unexpected in light of the prior art cited by the Examiner in establishing the patentability of the process claimed invention thereover.

Reconsideration of the present application and passing through the issues is respectfully solicited.

Respectfully submitted,

  
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TABLE

		U.S. 10/533 217				Comparative		Comparative		Comparative	
		Ex. 1	Ex. 2	Ex. 3	Comparative Ex. 1	Ex. 4	Ex. 2	Ex. 2	Ex. 18	Ex. 18	
Separating Agent (crosslinking method)	AS ( $\gamma$ ray)	AS ( $\gamma$ ray)	AS ( $\gamma$ ray)	AS (not crosslinked)	AS ( $\gamma$ ray) washed with THF	AS ( $\gamma$ ray) washed with THF	AS (not crosslinked) washed with THF	AS (not crosslinked) washed with THF	AS (UV)	AS (UV)	
$\alpha$ modification 1	Racemic	1.34	1.35	1.34	1.47	1.0	1.0	1.0	1.0	1.0	
	Racemic modification 2	2.3	2.31	2.34	2.47	1.58	1.0	1.0	1.40	---	
	Racemic modification 3	2.41	2.44	2.4	2.26	2.05	1.0	1.0	1.85	---	
	Racemic modification 4	2.12	2.12	2.09	2.88	1.68	1.0	1.0	1.50	---	

		U.S. 10/533 217				Comparative		Comparative		Comparative	
		Ex. 6	Comparative Ex. 3	Ex. 7	Ex. 4	Ex. 4	Ex. 17	Ex. 17	Ex. 17	Ex. 17	Ex. 17
Separating Agent (crosslinking method)	AD ( $\gamma$ ray)	AD (not crosslinked)	AD ( $\gamma$ ray) washed with THF	AD ( $\gamma$ ray) washed with THF	AD (not crosslinked) washed with THF	AD (not crosslinked) washed with THF	AD (UV)	AD (UV)	AD (UV)	AD (UV)	AD (UV)
$\alpha$ modification 1	Racemic	3.24	3.11	2.56	1.0	1.0	1.61	1.61	1.61	1.61	1.61
	Racemic modification 2	1.24	1.28	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Racemic modification 3	1.71	1.79	1.42	1.0	1.0	---	---	---	---	---
	Racemic modification 4	1.3	1.31	1.19	1.0	1.0	---	---	---	---	---

AS: Amylose tris[(S)-phenylethylcarbamate]      AD: Amylose tris(3,5-dimethylphenylcarbamate)